DIFFERENTIAL UPTAKE OF NON-FOULING PARTICLES BY PRIMARY HUMAN NEUTROPHILS

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The advent of targeted drug carriers has opened many new avenues for the delivery of therapeutics directly to the site of disease, reducing systemic side effects and enhancing the efficacy of therapeutic molecules. However, the packaging of therapeutics into particulate carriers for delivery comes with its own set of challenges and barriers. Among these, a great deal of research effort has focused on protecting carriers from clearance by phagocytes by altering carrier surface chemistry. Many groups have explored the use of polyethylene glycol (PEG) chain coatings to mitigate unwanted phagocytosis, as PEG is highly hydrophilic and is well-known for its anti-fouling propertiesNotably, very few papers have explored the effects of PEG on uptake by freshly obtained primary human phagocytes in physiological conditions, creating a disconnect between the prevailing literature and ultimate applications. In this work, we investigate the effect of PEGylation on uptake by primary human neutrophils *in vitro*, and compare these effects to several cell lines and other model phagocytic cells systems in evaluating the effects of surface chemistry on phagocytosis. We find that primary human neutrophils preferentially phagocytose PEGylated drug carriers, and that this effect is linked to factors present in human plasma. These findings have major implications for the efficacy of PEGylation in designing long-circulating drug carriers, as well as the need for thorough characterization of drug carrier platforms in a wide array of *in vitro* and *in vivo* assays.

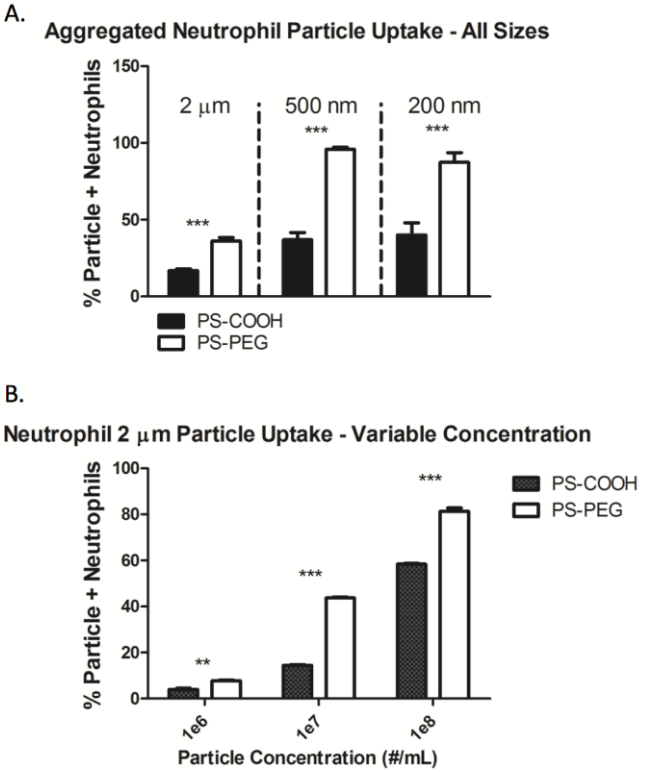

Figure 1 – (A) Aggregated particle uptake by primary human neutrophils for carboxylated and PEGylated 2 μm, 500 nm, and 200 nm polystyrene particles. (B) Particle uptake by primary human neutrophils for carboxylated and PEGylated 2 μm polystyrene particles at concentrations of 1E6/mL, 1E7/mL, and 1E8/mL